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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/190,138	11/12/1998	H. WILLIAM BOSCH	029318/0109	6300

7590 01/14/2004

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EXAMINER	
BERKO, RETFORD O	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/190,138	BOSCH ET AL.	
	Examin r	Art Unit	
	Retford Berko	1615	

-- The MAILING DATE of this communication appears on th cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *11-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *11-121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Acknowledgement: Receipt is acknowledged of applicant's response filed June 24, 2003.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-34, 40, 41, 44, 45, 47, 48, 51-62, 69-96 and 111-119 remain rejected under 35 U.S.C. 103 (a) as being obvious and therefore unpatentable over Edwards et al (US 5, 985,309).

Applicant's claims are directed toward a dry powder aerosol composition comprising spherically shaped aggregates formed from spray-drying aqueous dispersions of nanoparticulate drug particles, less than 1000 nm in size and wherein the aggregates are less than 100 microns in diameter.

Applicant's arguments have been considered and found unpersuasive. Applicant argues that Edwards does not teach or suggest spherical, dry powder composition of nanosize drug particles, contending that Edwards only teaches rough and amorphous non-spherical drug particles. Contrary to applicant's assertions, it is the examiner's position that the prior art as known and expressed in Edwards teaches smooth and spherical microparticle drug for inhalation (col 9, lin 11-21).

Applicant argues that the claimed dry powder aerosol comprising aggregates of spherical drug particles is a significant advance over the non-spherical single particles of drug because according to applicant, the spherical shape of particles positively influences aggregation of drug

particles and that this is crucial for the initial impact of the drug particles in the upper respiratory tract and subsequent retention in the lung. It is the examiner's position delivery of the drug, whether in the form of aggregates or single particles is a matter of choice and design and that the key issue is delivering the drug in a form that can reach the alveoli of the lung. It is the examiner's position that Edwards disclosed that nanosize drug particles in aerosol form were delivered to the alveoli of the lungcol 3, lin 330-35 and col 5, lin 30-40).

Applicant asserts that the aerodynamic behavior of non-spherical drug particles would present poor airflow to upper airways of the respiratory tract. The examiner disagrees with applicant's position as applicant provides no evidence establishing the assertion. Moreover, Edwards teaches that the nanosize drug particles in aerosol formulation can be effectively delivered to the alveoli of the lung (abstract; col 5, lin 35 and col 10, lin 35-45).

Applicant contends that the nanoparticle drug aggregates in a liquid medium must be able to redisperse in order to establish contact with and be absorbed by the nasal and lung tissues arguing that there is no teaching or suggestion in Edwards that the drug particles redisperse upon contact with liquid medium. Examiner posits that applicant claims nanoparticles of drug and not a liquid dispersion medium. In this regard, it is noted that applicant indicates no specific liquid medium for dispersion of drug particles. Furthermore, examiner disagrees with applicant's position because the disclosures in Edwards teach that the drug particles may be fabricated with appropriate material, surface roughness, diameter and tap density for localized delivery to selected regions of the respiratory tract (col 10, lin 45-55) including delivery to the alveoli (col 10, lin 35 and col 28, lin 35-40).

Claims 11-34, 40-45, 47, 48, 51-62, 65-96 and 97-199 remain rejected under 35 U.S.C. 103 (a) over Edwards (US 5, 985, 309) in view of Liversidge (US 5, 145, 684). Applicant argues that Liversidge does not disclose aerosol formulation of nanoparticle drugs; contending that the teaching in Edwards disclose significant difficulties respecting aerosol preparation and delivery.

Examiner disagrees with applicant's position because the disclosure in Edwards teaches: (1) incorporation of surfactants into the drug particles thereby effectively reducing the tendency of the particles to agglomerate (col 7, lin 20-45) and (2) the effective delivery of the drug particles in the lung col 9, lin 40-60 and col 10, lin 35-45).

While the disclosures in Leversidge hint of some level of agglutination of drug particles (col 4, lin 60-65), it is the examiner's position that overall, the disclosures in Leversidge: (a) are in the same field of endeavor as that in Edwards—nanosize drug particles that are surface modified in liquid dispersion (col 3, lin 45) and (b) address similar problems that were raised in Edwards concerning nanosize drug delivery formulations through the respiratory tract and therefore inhalation (col 5, lin 1 and clo 12, lin 50).

Claims 35, 36, 49, 63 and 64 remain rejected under 35 U.S.C. as being unpatentable over Edwards et al (Patent '309) in view of Dalby et al (US 5, 202, 110).

Applicant contends that neither Edwards nor Dalby (ither singly, or in combination) teach or suggest aerosol composition of nanosize drug particles. Examiner disagrees with applicant's position in that the teaching in Edwards regarding spherical, nanosize aerosol particles of drug was discussed above (col 4, lin 40-45 and col 9, lin 65). Dalby was relied on as teaching the propellant or aerosolized formulation for delivery of nanosize beclomethazone particles, albeit no chlorofluorocarbon was used (col 7, lin 10, continuing to col 8, lin 25).

In traversing the rejection of claims 120 and 121 as unpatentable over Edwards (Patent '309) in view of the secondary reference, Goodman and Gilman (Goodman, Pharmacological Basis of Therapeutics, page 666, 9th ed, 1996), applicant argues that while Edwards does not teach or suggest the claimed aerosol composition, that Goodman also fails to address the issue regarding benefits for delivering drugs nanoparticles in aggregate formulation. Examiner diagrees with applicant's position in light of the discussion respecting the teachings in Edwards and further notes that Goodman teaches aerosolized formulation of glucocorticoids for delivery by inhalation. (see page 666, first and second paragraphs).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Retford Berko whose telephone number is 703-305-4442. The examiner can normally be reached on M-F at 8:00 a.m.-5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9903 for regular communications and 703-746-9903 for After Final communications.

An inquiry of a general nature or relating to the status of this communication or proceeding should be directed to the receptionist whose telephone number is 703-308-1243.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600